

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY


(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

REC'D 06 JAN 2006

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Applicant's or agent's file reference P182	<b>FOR FURTHER ACTION</b> See Form PCT/PEA/416	
International application No. PCT/GB2004/002909	International filing date (day/month/year) 05.07.2004	Priority date (day/month/year) 04.07.2003
International Patent Classification (IPC) or national classification and IPC A61K38/10, A61K38/17, A61P37/02		
Applicant ABERDEEN UNIVERSITY et al.		
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> sent to the applicant and to the International Bureau) a total of 2 sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>		
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>		
Date of submission of the demand  04.05.2005	Date of completion of this report  05.01.2006	
Name and mailing address of the International preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer  Merckling-Ruiz, V  Telephone No. +49 89 2399-8590	



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**INTERNATIONAL PRELIMINARY REPORT  
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International application No.  
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**Box No. I Basis of the report**

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
  - ☐ publication of the international application (under Rule 12.4)
  - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements\*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

**Description, Pages**

1-15 as originally filed

**Claims, Numbers**

8 received on 09.05.2005 with letter of 04.05.2005  
1-7 filed with telefax on 05.10.2005

**Drawings, Sheets**

1-8 as originally filed

☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing (*specify*):
  - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing (*specify*):
  - ☐ any table(s) related to sequence listing (*specify*):

\* If item 4 applies, some or all of these sheets may be marked "superseded."

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**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

Novelty (N)	Yes: Claims	1-8
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-8
Industrial applicability (IA)	Yes: Claims	1-8
	No: Claims	

2. Citations and explanations (Rule 70.7):

**see separate sheet**

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1. Reference is made to the following documents :

- D1: WATKINS N.A. ET AL.: "HPA-1a phenotype-genotype discrepancy reveals a naturally occurring Arg93Gln substitution in the platelet beta-3 integrin that disrupts HPA-1a epitope." BLOOD, vol. 99, no. 5, 1 March 2002 (2002-03-01), pages 1833-1839, XP002304950
- D2: WO 90/12593 A (BLOOD CENTER OF SOUTHEASTERN W) 1 November 1990 (1990-11-01)
- D3: WO 90/00178 A (COR THERAPEUTICS INC) 11 January 1990 (1990-01-11)
- D4: WO 93/12127 A (SCRIPPS RESEARCH INST) 24 June 1993 (1993-06-24)

Unless specified otherwise, the relevant passages are the ones that are cited in the Search Report.

**Regarding point V**

2. Neither D2 nor any other available prior art document discloses the use of an immunologically effective platelet protein or peptide fragment for the manufacture of a medicament for preventing/managing conditions caused by exposure to an antithetical allele of a platelet, **wherein said medicament is formulated for delivery through non-invasive routes**. In D2, the use of such peptides is based on their ability to block passively pathogenic antibodies, so that the peptides should be administered to blood via a systemic route (see page 17 lines 15-19 of D2). Claims 1-5 and 7 are novel.
- 2.1 Claims 6 and 8 are novel because there is no document disclosing the same medical use of the same specific peptide sequences.
3. The technical problem solved by the present application is to provide a medicament for treating/preventing conditions elicited by exposure to an antithetical allele of a platelet,

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by transfusion or by pregnancy.

The solution to this problem is allegedly the administration through non-invasive routes of "an immunologically effective platelet protein" (or a peptide fragment thereof).

D4 shows that the same epitopes as in the present application (see Seq. No.5, 7 and 11 of D4, identical to Seq. No.2 of application, for example) can be used for eliciting antibody responses and even for manufacturing such antibodies. These peptides are shown to be "immunologically effective" in D4, since "immunologically effective" is not restricted to T cell response.

Even if neither D2 nor D4 suggest to administer these epitopes in a non-invasive manner, it should be emphasized that the only demonstrated technical effect of the present application is that the peptidic epitopes induce T cell proliferation in vitro. Inventive step can therefore not be acknowledged on the sole basis of a new route of administration since no administration route has been tested.

Moreover, it is submitted that not all embodiments of claim 1 exhibit the desired technical effect : the wording "immunologically effective platelet protein" defines a protein in terms of result to be achieved which does not allow the skilled person to determine which proteins or peptides are encompassed in this claim. The only peptides that were adequately disclosed and supported by the present application are proteins/peptides containing the P1<sup>A</sup> determinant of GPIIb. No technical effect has been demonstrated for any other peptides/proteins that fall under the scope of this very broad claim.

In conclusion, claims 1-8 are not inventive.

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### Claims

- 5 1. Use of an immunologically effective platelet protein or a peptide fragment thereof in the manufacture for a medicament for the prevention or management of a condition caused by exposure to an antithetical allele of a platelet by transfusion or during pregnancy by tolerisation wherein the  
10 medicament is formulated for delivery through non-invasive routes.
2. Use according to claim 1 wherein the condition is fetomaternal alloimmune response thrombocytopenia (FMAIT),  
15 post-transfusion purpura or platelet refractoriness.
3. Use according to either claim 1 or 2 wherein the platelet protein is a human platelet antigen (HPA).
- 20 4. Use according to claim 3 wherein the HPA is selected from HPA-1a, HPA-1b, HPA-2a, HPA-2b, HPA-3a, HPA-3b, HPA-4a, HPA-4b, HPA-5a, HPA-5b, HPA-6a, HPA-6b, HPA-7a, HPA-7b, HPA-8a, HPA-8b, HPA-9a, HPA-9b, HPA-10a, HPA-10b, HPA-11a, HPA-11b.
- 25 5. Use according to claim 4 wherein the HPA has a genotype HPA-1a.
6. Use according to claim 5 wherein the HPA-1a has sequence SEQ ID No:1, 2, 3, 4, 5, 6 or 7.
- 30 7. Use according to any preceding claim wherein the composition is formulated for delivery through mucosal tissue.

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8. Use as substantially hereinbefore described with reference to Figure 1 in the manufacture for a medicament for the prevention or management of a condition by tolerisation caused by exposure to an antithetical allele of a platelet by 5 transfusion or during pregnancy.

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AMENDED SHEET